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Docosahexaenoic acid supplementation (DHA) and the return on investment for pregnancy outcomes¹²³

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Abstract

The Kansas University DHA Outcomes Study (KUDOS) found a significant reduction in early preterm births with a supplement of 600 mg DHA per day compared to placebo. The objective of this analysis was to determine if hospital costs differed between groups. We applied a post-hoc cost analysis of the delivery hospitalization and all hospitalizations in the following year to 197 mother-infant dyads who delivered at Kansas University Hospital. Hospital cost saving of DHA supplementation amounted to \$1678 per infant. Even after adjusting for the estimated cost of providing 600 mg/d DHA for 26 weeks (\$166.48) and a slightly higher maternal care cost (\$26) in the DHA group, the net saving per dyad was \$1484. Extrapolating this to the nearly 4 million US deliveries per year suggests universal supplementation with 600 mg/d during the last 2 trimesters of pregnancy could save the US health care system up to USD 6 billion.

Keywords

docosahexaenoic acid; pregnancy; hospital cost; preterm birth

INTRODUCTION

Preterm birth is defined as birth prior to 37 weeks gestation and in 2013 (the most recent data available) preterm birth accounted for 11.4% of the nearly 4 million births in the US [1]. Perinatal health care costs are significant among preterm neonates [2], but are particularly high for infants born before 34 weeks gestation (called early preterm birth or

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ePTB), who accounted for ~3% of US 2014 births. Two recent randomized trials of DHA supplementation in pregnancy found that women assigned to a relatively large supplement of DHA had a significant reduction in EBP compared to the placebo group [3, 4]. A recent meta-analysis by Kar et al. [5] included 6 trials that evaluated the effect of omega-3 fatty acid supplementation on ePTB and concluded omega-3 fatty acids reduced ePTB by 58%.

An analysis of hospital cost from the DHA to Optimize Mother and Infant Outcome (DOMInO) trial conducted in Australia and published in this journal last year determined DHA supplements could decrease individual hospital costs by AUD 92 with a savings to the public hospital system of between AUD 15 and 51 million per year [6]. In the US, the incidence of ePTB is higher than in Australia. That coupled with a larger number of US pregnancies per year suggests cost savings of DHA supplementation could be even more substantial in the US. Our objective was to determine the hospital costs for a subset of mother-infant dyads in the Kansas University DHA Outcomes Study (KUDOS) and to estimate the possible national hospital cost and net savings after including the cost of universal supplementation with 600 mg DHA per day for 26 weeks of pregnancy. We extrapolated these results to suggest the potential savings to the US health care system of supplementing all US pregnant women with 600 mg per day of DHA.

SUBJECTS AND METHODS

Pregnant women who enrolled in KUDOS and their newborn infants are the subjects of this study. Trial results of DHA supplementation on pregnancy outcomes have been reported elsewhere [4]. Briefly, women were randomly assigned to consume 3 capsules per day containing either a placebo (corn and soybean mixture) or a total of 600 mg DHA (DHASCO, DSM, Baltimore, MD) from a mean of 14.5 weeks gestation until they gave birth. Enrollment occurred between 2006 and 2010 and all participants were from the Kansas City Metropolitan Area, which has a population of approximately 2 million people. Participants for whom delivery data were available self-identified as Black (42%) or from another race (61.2%). While we did not find a significant reduction in birth before 37 weeks (8.8 vs 7.8% in the placebo and DHA groups, respectively), there was a significant reduction in ePTB (4.8 vs. 0.6% for placebo and DHA groups, respectively). Additionally, we did not find overall differences in the rate of admissions to a neonatal intensive care unit (NICU), but infants in the placebo group admitted to the NICU spent a mean of 38.4 days in hospital compared to 7.8 days for the DHA group admitted to the NICU [4].

To address our objective of examining hospital costs, we applied a post-hoc cost analysis to the subset of mother-infant dyads (n=197) from the trial who delivered in the Kansas University Hospital and had available admission data. We included cost incurred at the time of birth as well as cost that occurred for the mother and/or baby for any hospital readmissions in the year following initial hospital discharge. We used the Diagnosis Related Group (DRG) for each admission to assign cost from the HCUP Nationwide Inpatient Sample for 2010 (U.S. Department of Health and Human Services: Agency for Healthcare Research and Quality. (2015). *Healthcare Cost and Utilization Project (HCUP)* [Data file]. Available from: <http://hcupnet.ahrq.gov/>). Because inpatient utilization data from surrounding hospitals was not available, we could not obtain the DRG and assign costs to

104 mother-infant dyads that participated in the study but delivered outside of the University hospital.

Statistical comparisons between groups were done by simple t-test for means or simple linear regression.

The cost of providing each woman with a DHA supplement of 600 mg per day for the last 26 weeks of pregnancy was also calculated. Cost was determined by the average retail price of three on-line websites (21st Century Prenatal DHA, Nordic Natural Prenatal and GNC DHA 600) and averaged \$166.48/pregnancy or \$6.40/week. We calculated cost, cost-benefit ratio, net benefit, net benefit ratio and return on investment associated with the use of DHA supplementation.

RESULTS

Demographic and hospital resource use are shown in **Table 1**. Demographic data did not differ between the subset with admission data at Kansas University Hospital and women enrolled in the study who gave birth at other hospitals in the Kansas City Metropolitan Area (n=53 and 51, respectively for placebo and DHA-supplemented groups, data not shown).

In considering the infants, there was a hospitalization cost savings of \$1678 in the DHA-supplemented group compared to the placebo group for birth and readmissions in the first year. Based on the estimated cost of supplementation, the cost-benefit ratio was 10.1:1 meaning that for every dollar invested in DHA supplements, there was a 10.1 -fold return in hospital cost savings for infants in the first year. Even reducing the savings by the cost of providing all pregnant women with 600 mg per day of DHA from 14 weeks gestation until birth, the net cost benefit would be a savings of \$1512 per infant or an overall return of 9.1 or 910%.

We also assessed the hospitalization costs for mothers to determine if the cost for mothers' hospitalization differed by group. Regarding mothers only, overall delivery and readmission costs were \$26 higher in the DHA-supplement group as compared to the control.

Infants in the control group had longer lengths of stay and perinatal hospitalization costs, though not significantly ($p = 0.215$ and $p = 0.441$). As expected, admission to the NICU was related to a significant increase in length of stay (NICU coefficient = 20.41, t -test = 7.764, $p = 0.0000$), however, there was not a differences between the groups in NICU admissions, which were actually somewhat higher in the DHA group (7.4% placebo, 10.7% DHA). For infants admitted to the NICU, however, the length of stay was longer in the placebo group and the difference between the groups approached statistical significance: group coefficient = 2.907, t -test = 2.907, $p = 0.057$.

We don't have details of the procedures more common in the highest 10% of cost users as the costs were assigned at the DRG level. The range was the same in both groups, with roughly 70% of each treatment arm having the lowest DRG cost (\$972) while 1.9% of the DHA group had the highest DRG cost (\$60,302) and 4.3% of the placebo group had the highest DRG cost (\$60,302).

A higher percentage of infants and mothers in the placebo group compared to the DHA group were re-hospitalized during their first year of life. Combined index and readmission costs for mother-infant pairs totaled $\$8,615 \pm 11,331$ and $\$10,267 \pm 17,503$ for the DHA-supplemented and control group, respectively ($p = 0.429$).

DISCUSSION

Applying this analysis to 3,988,076 live births in the US in 2014 (the latest year for which figures are available) [1] suggests a potential savings of USD 6.60 billion for hospital costs and a net savings of USD 5.94 billion to the US health care system if all pregnant women were provided with 600 mg of DHA per day during the last 26 weeks of pregnancy. Even after adding the slightly higher cost for hospitalization of women supplemented with DHA to the lower cost of hospitalization for infants of DHA-supplemented mothers, the difference between the groups still results in a potential hospital savings of USD 6.50 billion and the net savings USD 5.84 billion nationally.

Overall differences in hospitalization resources, while not statistically significant, were consistent with the primary trial findings [4]. DHA resulted in appreciable savings in this cohort. The magnitude of the cost offset in this small study suggests the potential for a substantial return on investment with widespread use of DHA supplementation during pregnancy. The amount that DHA supplementation reduced the average cost of infant hospitalization is particularly large given that most pregnancies in both groups were uncomplicated and had a much lower cost. These normal deliveries also contributed to the large error term for mean cost.

If similar differences were found in other US pregnancies, the potential savings to the health care system would be in the neighborhood of USD 6.6 billion. This number could be conservative as costs for ePTB alone increased substantially between 2010 and 2013, the latest year for which figures are available (<http://hcupnet.ahrq.gov/>). The difference between mean national cost for a normal newborn delivery and the at most risk premature delivery increased from USD 79,260 in 2010 to USD 96,676 in 2013. With an estimated 110,000 ePTB in 2013, the additional cost for these births alone currently comes close to USD 10.6 billion.

The most recent ePTB rate in the US for all races is 2.75%, down from 2.96% in the years KUDOS was conducted. Interestingly, if we assume this rate and the 58% reduction in ePTB by long chain omega-3 fatty acid supplementation observed in the Kar et al. [5] meta-analysis, we come up with a potential savings of USD 6.15 billion for ePTB alone based on an estimated current cost of ePTB of USD 10.6 billion. The savings could be even higher if one considers subsequent long-term expenditures for special education services associated with disabling conditions common among premature infants. For example, Mangham et al. [7] estimated the full cost for all preterm infants and for very preterm and extremely preterm infants in the UK from birth to 18 years of age. The total cost of PTB using 2006 figures from the UK was USD 4.567 billion with 92% of cost related to the birth hospitalization.

Forty-two percent of the women enrolled in KUDOS were Black [4] which is higher than the national average of 16%. This could overstate our estimated finding because Black women in the US are more likely to have PTB and ePTB (4.6% in 2014) (<http://hcupnet.ahrq.gov/>). Their rate of ePTB is similar to the rate of 4.8% we found in the placebo group of KUDOS. White and Asian women in the US have rates of ePTB of 2.4 and 2.2%, respectively, very close to the 2.25% observed in the placebo group of DOMInO.

The DOMInO study cost analysis found that the reduction in cost with DHA supplementation was driven by reducing the number of infants with the lowest cost associated with birth and not with reducing premature births [6]; however, we find no difference between the groups in the proportion of births with the lowest DRG cost, and a near significant difference favoring DHA supplementation in reducing births with the highest DRG cost.

While we undertook this analysis because of the reduction in ePTB in the KUDOS trial, the overall number of pregnancies assessed is relatively small and the number of ePTB in the study was small. Moreover, the majority of ePTB in the placebo group were not among the pregnancies available for this cost analysis as 4 of the 7 ePTB deliveries took place in other hospitals in the Kansas City Metropolitan Area. Therefore, we do not believe a strong conclusion can be drawn that the differences in cost we observed are due to a reduction in ePTB in the DHA group.

A strength of our analysis is that we included costs for maternal hospitalization for the birth and the year following birth; and reduced the estimated savings by the cost of providing the DHA supplement used in KUDOS.

Ahmed et al. [6] conclude that a public policy effort to increase DHA intake of pregnant women could save up to AUD 51 million. We determined here that a similar public policy in the US could potentially generate savings of more than USD 6 billion. In conclusion, we agree with our Australian colleagues who conducted the DOMInO trial [3] and cost analysis [6] that a public health policy to increase DHA intake during pregnancy could result in significant cost savings to the health care system in our country.

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abbreviations

DHA	docosahexaenoic acid
DRG	diagnosis-related group
ePTB	early preterm birth
HCUP	healthcare cost and utilization project

KUDOS Kansas University DHA outcomes study

DOMInO DHA to Optimize Mother and Infant Outcome

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Highlights

- Early preterm birth (ePTB) occurs before 34 weeks gestation
- ePTB cost the US approximately USD 10.6 Billion in 2014
- Public policy effort to increase DHA intake of pregnant women has the potential to save the US healthcare system more than USD 6 billion.

Table 1

Descriptive statistics and event and cost outcomes for mothers and infants

	Mothers		Infants	
	DHA supplemented	Control	DHA supplemented	Control
Number of cases	103	94	103	94
Gestation at delivery (wks)	39.4	39.1	-	-
Maternal age (years)	25.4	24.9	-	-
Maternal race				
Black	38.8%	45.7%	-	-
White	59.2%	53.2%	-	-
Other	1.9%	1.1%	-	-
Maternal education (years)	13.7	13.3	-	-
Income by zip code (\$)	\$44,193	\$40,713	-	-
Prenatal vitamin supplementation	98.1%	98.9%	-	-
Elected additional DHA supplementation	5.8%	10.6%	-	-
Early preterm birth (n)	1	3	-	-
Gestational diabetes	4.9%	4.3%	-	-
Pre-eclampsia	1.9%	2.1%	-	-
C-Section delivery	31.1%	28.7%	-	-
Vaginal delivery	68.9%	71.3%	-	-
Complicated delivery	30.1%	22.3%	-	-
Infant gender, male	-	-	51.5%	53.2%
Normal newborn	-	-	69.9%	68.1%
Length of stay (days), index	2.7 (1.3)	2.7 (2.6)	2.8 (3.7)	5.1 (17.1)
Index hospital costs, mean (std dev)	\$4,292 (1,446)	\$4,087 (1,424)	\$3,208 (8,879)	\$4,378 (12,265)
Readmitted within 12 months (%)	2.9%	6.4%	6.8%	9.6%
Sum hospital costs, mean (std dev)	\$4,474 (1,885)	\$4,448 (2,184)	\$4,141 (11,134)	\$5,819 (16,580)